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FLUORINE COMPOUNDS IN ORGANIC SYNTHESES

BY

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FLUORINE
Compounds in Organic Syntheses

Not much has been heard of the impact of the new tool, fluorine and its compounds, upon the synthetic c h e m i c a l industry, nevertheless the effect has been widespread and of vital importance in such wartime applications as 100-octane aviation gasoline and insecticides. In this article the author discusses the two-fold use of fluorine, first, the introduction i n t o other chemicals, and second, its use as a catalyst. The discussion may suggest other means of using this material to make new products. —*Editors*

COMMERCIAL development of the Freon refrigerants in 1930 and the more recent development of the "alkylate" for 100-octane aviation gasoline strikingly illustrate the impact of a new tool, fluorine chemistry, upon the synthetic organic industry. These developments represent two entirely different roles played by fluorine compounds, and are harbingers of what can be expected in the future. In the first instance, the Freons are organic fluorine compounds, and in the latter, the aviation alkylate does not contain fluorine in its molecules but depends upon hydrogen fluoride as a catalyst in its synthesis. The object of this discussion is, first, to describe briefly these processes and other commercial developments, second, show by these illustrations that further developments are now within the scope of good commercial practice, and third, point out the almost unlimited field of research that may lead to many important developments.

In this new research the "key chemical"

is hydrofluoric acid (aqueous and anhydrous). It enters directly or indirectly into almost every process of fluorine chemistry, therefore a thorough understanding of its physical and chemical properties is a prime prerequisite. The production, handling, and properties of this chemical have been covered thoroughly in the literature, therefore will not be discussed in this article.

REFRIGERANTS

The initial industrial achievement in organic fluorine chemistry came when Midgley and Henne in 1930 announced the commercial production of new refrigerants, Freons. They put into industrial practice a chemical reaction discovered in 1892 by Swarts, a Belgian chemist. The Swarts reaction, in its simplest terms, involves the replacement of chlorine by fluorine in a suitable organic compound by means of anhydrous antimony trifluoride. In some cases, antimony pentachloride is necessary. The reaction has been extended considerably as to catalysts, types of compounds that can be prepared, and the fluorinating agents involved.

Freons are chlorofluoro derivatives of methane and ethane, and are prepared from carbon tetrachloride, chloroform, and hexachloroethane depending upon the compound desired. For illustrative purposes, the commercial synthesis of dichlorodifluoromethane (F-12) is described. Carbon tetrachloride and anhydrous hydrofluoric acid (correctly called hydrogen fluoride) are fed continuously into a heated reactor containing the anhydrous antimony halide. The reaction products pass into a fractionating column where the free acids (HCl and HF) are separated from the Freon and the insufficiently fluorinated raw material is returned to the system. This fractionation is simple as, for example, in the case of carbon tetrachloride, where each substitution of a fluorine for a chlorine atom is accompanied by a lowering of the boiling point of about 52 deg. C. By means of scrubbing and drying towers

the final product is condensed. It is sold in cylinders or in carload lots. The active fluorinating agent or catalyst, antimony trifluoride, is continuously regenerated.

Freon is a trade name of Kinetic Chemicals Co., for the new refrigerants. Since there are a number of these compounds, they are differentiated by symbols. The most common is F-12, CCl_2F_2 (loosely spoken of as Freon), in addition, there is F-11, CCl_3F; F-21, $CHCl_2F$; F-22, $CHClF_2$; F-113, CCl_2FCClF_2; and F-114, $CClF_2CClF_2$. Due to their outstanding properties of stability, non-toxicity, non-flammability, and non-corrosiveness they are used extensively in refrigeration and air-conditioning equipment.

Fumigation of tents, barracks, airplanes, tanks and military installations, especially in the tropics, has become a simple operation as the result of a new aerosol fumigator called "bug bomb." Such insects as mosquitoes, flies and other disease carriers are readily exterminated in a matter of several minutes. This bomb, which can be carried in one hand, contains a mixture of pyrethrum, sesame oil, and liquid Freon. All of the components are harmless to humans. By opening the ejection valve, the Freon begins to boil (its boiling point is about —19 deg. F.) expelling the insecticidal mixture and virtually exploding it as a fine mist which remains suspended in air for a long time. One bomb contains sufficient material to fumigate a space of 150,000 cu.ft. Over 7,000,000 of these bombs have been delivered to the Armed Services. Already postwar plans call for their use in civilian life, and it has been suggested that a new paint gun using this principle be developed for spray painting. The production of Freon upon completion of two new plants will be approximately 2,400 tons per month.

AVIATION GASOLINE ALKYLATE

The most recent and distinguished work in organic synthesis involving fluorine chemistry is the preparation of "alkylate" for 100-octane aviation gasoline by hydro-

gen fluoride alkylation. The discovery of this process by Ipatieff and his coworkers in the Universal Oil Products laboratories, and the initial plant installation by the Phillips Petroleum Co. in 1942 is of inestimable value to the war effort in respect to air supremacy. Due to war restrictions, details on this process are not available, but the essential principles are known.

The process is essentially the conversion of olefines in the presence of isoparaffins to saturated products with anhydrous hydrofluoric acid as a catalyst. Usual engineering materials are employed for corrosion is not a serious factor so long as moisture is excluded.

A thoroughly mixed feed stock of olefines and isoparaffins is fed into an alkylation chamber containing anhydrous hydrofluoric acid. Since HF is quite insoluble in the hydrocarbon mixture and since considerable heat of reaction is evolved in the alkylation, the chamber is equipped with suitable stirring equipment and cooling coils. The reaction products are passed into a separating tank to allow the HF to separate as a lower layer and be returned to the alkylation chamber. From the separating tank, the hydrocarbon mixture is passed successively into a HF stripping column, a dehydrofluorinator, a de-isobutanizer, a debutanizer, and finally through a fractionating column to give the desired alkylate fraction. Since the alkylation is a liquid phase reaction, it is necessary to maintain sufficient pressure so that the reacting components remain in a liquid state.

The alkylate is a mixture of branched methyl side chain isomers of heptane, octane, etc. The 100-octane aviation gasoline may contain from 25 to 40 percent of this alkylate. Triptane, 2, 2, 3-trimethylpentane, recently announced as the most powerful aviation fuel component known, can also be made by this process, but in very low yields.

In addition to the desired reaction in the alkylation chamber, a variety of other reactions take place such as de-alkylation, polymerization and depolymerization, hydrofluorination and dehydrofluorination, hydrogen transfer, and isomerization. All of these reactions must be taken into consideration in order to obtain the most favorable yield. Without a doubt, this process with its numerous reactions is an excellent example of the versatility of hydrogen fluoride in organic chemistry, and a thorough knowledge of these reactions should lead to many other interesting developments.

DYES

Shortly after the appearance of the Freon refrigerants, the I. G. in Germany introduced a new series of fast Naphthol AS type dyes which contained fluorine in their molecules. Some of these dyes ap-

peared on the American market. The print dyes exhibit unusual clearness in color (mostly yellow, orange and red) and possess excellent light fastness. It has been stated that one of the red colors meets German Government specifications for use in the official banner. In general, they are coupled products of a Naphthol AS type with fluorine containing diazotized bases as used in the recently developed Rapidogen colors for printing cotton goods. Fast Orange Salt RD is probably a representative of one of the diazotized bases. The diazotized bases are supposedly derivatives of benzotrifluoride (a fluorine analog of benzotrichloride):
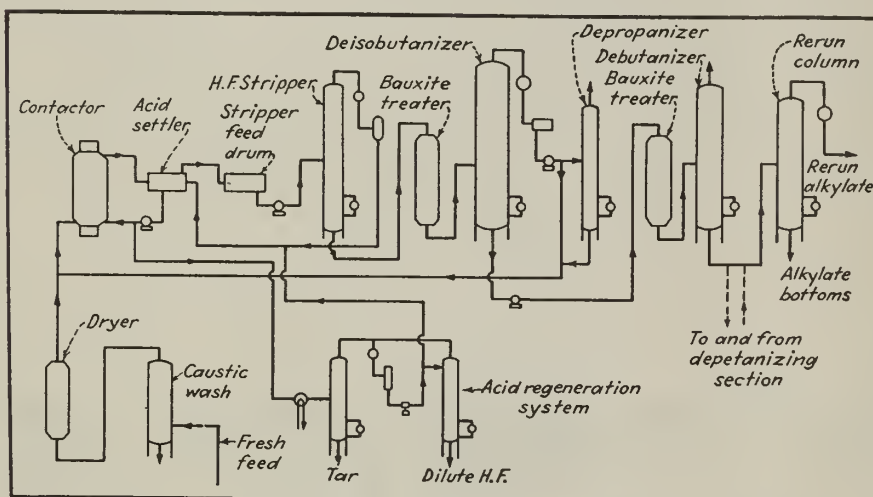
BENZOTRIFLUORIDE

Since benzotrifluoride ($C_6H_5CF_3$) can be considered as the parent of these dyes, a brief discussion of its synthesis and properties is apropos. The fluorine is present in the form of a —CF_3 group. This group in contrast to its chlorine analog, —CCl_3, is very stable, does not hydrolyze under ordinary conditions, and many of the usual reactions used in the synthesis of dye intermediates have no deleterious effect upon it. Benzotrifluoride can be prepared

from benzotrichloride by the Swarts reaction in the absence of a catalyst. Commercially, anhydrous hydrofluoric acid is used in place of antimony trifluoride. The reaction takes place in an autoclave under heat and pressure resulting in an almost quantitative yield. The process is similar to the production of Freons.

In general, fluorine in the aromatic nucleus is quite stable and an effort has been made to develop dye intermediates possessing such a structure. None have found a place in the competitive market. However, a brief discussion of the introduction of fluorine into the aromatic

nucleus is pertinent as some of these syntheses may find industrial application. An aromatic amine may be converted to the corresponding fluorine compound by two methods. The first method involves the diazotization of the amine in highly concentrated or anhydrous hydrofluoric acid with sodium nitrite followed by decomposition to the fluorine compound. This synthesis can be carried out in iron equipment. An 87 percent yield has been reported for fluorobenzene from aniline.

SCHIEMANN REACTION

The second method involves the formation of an insoluble diazonium fluoborate (also called borofluoride) followed by a thermal decomposition to the corresponding fluorine compound. This method is known as the Schiemann reaction, unfortunately not named after its discoverers, but after the scientist who made an extensive study of its possibilities. When a soluble diazonium salt, most generally a chloride, is treated with fluoboric acid (HBF_4), a precipitate of the diazonium fluoborate is formed. The diazonium fluoborates are quite insoluble and surprisingly stable, thus it is possible to isolate and dry them. Since these salts can be readily isolated, many diazonium compounds can be purified as the fluoborate salts. Since these compounds have definite decomposition temperatures (usually not over 200 deg. C.), the dried salts can be thermally decomposed to the desired fluorine compound, with nitrogen and boron trifluoride being evolved as gases. Sodium fluoborate can be used in place of fluoboric acid thereby eliminating to a large extent the intrinsic corrosiveness of the acid and simplifying the method so that many aromatic fluoric compounds can be prepared

The most recent work in organic synthesis involving fluorine chemistry is the preparation of "alkylate" for 100-octane aviation gasoline by the hydrogen fluoride alkylation process

in ordinary laboratory glassware. In general, the yields are good; and, by recovering the boron trifluoride the cost can be materially reduced.

Stabilized diazo compounds in the form of complex double salts, etc., have been available for a long time. In a broad sense, the diazonium fluoborates are stabilized diazo compounds. For instance, Fast Red RL Salt, chemically known as 2-methyl-4-nitrobenzene diazonium chloride can be stabilized by conversion to the fluoborate salt. It is conceivable that some diazonium fluoborates may appear on the market as such. The most attractive feature of these compounds lies in the fact, that certain diazonium compounds too difficult to obtain in sufficient purity for dyeing can be readily purified through the fluoborate salts. It has been reported that borofluoro sulphonic acid, fluorosulphonic acid, and certain metallic fluorides also will form stabilized salts.

POLYMERS

Swarts in his studies on fluoroethylenes reported that a number of these compounds gave polymers of varying degrees of hardness. A striking example cited by him in 1909 was that α-bromovinylfluoride (CH$_2$ = CBrF) gave a "translucent block as hard as glass." Nothing further was done on this subject until a patent was issued to the I. G. in 1939 on some vinyl polymers that are described as nonflammable, insoluble in organic solvents, and very stable to chemical agents. In this group, trifluorovinyl-chloride exhibited these properties to the greatest extent.

Theoretically, tetrafluoroethylene should give the most stable polymer and in 1941 a patent was issued to the du Pont company on this polymer. In the latter patent, it was indicated that this polymer was fairly clear and transparent, and could be molded. There is no question that such a product will find some interesting applications.

The fundamental compounds for the synthesis of these polymers are directly related to the ethane type of Freons discussed earlier in this article. In general, the fluorinated olefines may be synthesized from an appropriate chlorofluoroethane by the removal of HCl or two adjacent chlorine atoms with well-known reactions. Halogen acid may be removed by various alkaline reagents.

The preferred reaction is the removal of two chlorine atoms on adjacent carbon atoms by zinc in a suitable solvent such as alcohol.

It is interesting to note that chlorine is preferentially removed over that of fluorine. Heat and pressure are sometimes necessary to obtain satisfactory yields. Since the higher fluorinated ethylenes are gases, they are synthesized and polymerized in closed systems.

In the case of non-fluorine polymers, boron trifluoride has been used as a catalyst in the synthesis of a rubber-like polymer from isobutylene. It is doubtful that BF$_3$ is being used in the present synthetic rubber program. The ability of HF as a catalyst in polymerizing olefines in rather common knowledge; also, certain vegetable oils are readily polymerized to a rubber-like material.

The fumigation of airplanes, tanks, and military installations has become a simple operation as the result of a new fumigator called an aerosol or "bug bomb." This bomb contains a mixture of pyrethrum, sesame oil and liquid Freon. Here containers are tested before being filled

ACETIC AND PROPIONIC ACIDS

One of the most important applications of boron trifluoride as a catalyst is in the new synthetic acetic and propionic acid process of the du Pont company. The catalyst is actually used in the form of a hydrate. The process is essentially a condensation of carbon monoxide with methanol or ethanol under pressures as high as 900 atmospheres at 260 deg. C. Yields of 79 percent for acetic and 50 percent for propionic acid are reported.

It is possible to effect many other condensations with this catalyst, particularly where an acid type of catalyst is required for the operation.

The question of the use of fluorine compounds as insulating and cooling oils for transformers and the like has been superficially investigated. Chlorinated paraffins and biphenyls are being used for this purpose and it is only natural to suspect that the fluorine compounds may be more stable. A number of patents have been issued covering the use of some of the chlorofluoroethanes (Freon derivatives) and chlorinated benzotrifluorides for this purpose. The possibilities have not been exhausted and practically no correlation data are available between constitution and such factors as dielectric constants, power factors, and the like.

PHARMACEUTICALS

Some interest has been indicated in medical and pharmaceutical fields. Unfortunately, little information is available on the physiological effect of organic fluorine compounds. In some cases they may be toxic and in others not. Fluoroform (CHF$_3$) is practically inert as far as anesthetic and physiological properties are concerned; as a matter of fact, it can be substituted for nitrogen in air with no apparent effect. In Germany, 3-fluorotyrosine was sold under the name of Pardinon for treatment of hyperthreosis; and an ointment Epidermin containing p. p'-difluorobiphenyl for the treatment of wounds and burns was also available. It has been indicated that p-fluorosodium benzoate can be used as an internal antiseptic as it is not as toxic as sodium fluoride.

Fluoroacetic, fluorobenzoic and fluorobenzene sulphonic acids have been suggested for use as fungicides, insecticides and disinfectants, but in most cases there is a question of their efficacy. Fluorostearic acid is reported to be as effective as certain copper preparations for mildew control. This compound is readily prepared by the addition of HF to oleic acid; the addition of HF to the double bond is rapid in contrast to HCl which combines very slowly. Outside of a few instances, the field of fungicides, insecticides, etc., is practically unexplored and should hold considerable promise for future investigations and developments.